Docket No. 3856-4006

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Reissue of:

U.S. Patent No. 5,556,838

David J. **MAYER** et al.

Filed: May 19, 1994

Granted: September 17, 1996

Serial No.: TBA

For: Inhibiting the Development of Tolerance to and/or Dependence on an Addictive Substance

Commissioner for Patents
U.S. Patent & Trademark Office
Washington, D.C. 20231

SIR:

REISSUE DECLARATION AND POWER OF ATTORNEY BY ASSIGNEE

I hereby declare that:

I. My residence, post office address and citizenship are stated below next to my name.

II. I am authorized to act in connection with the aforesaid patent on behalf of the assignee Virginia Commonwealth University.

III. The entire right, title and interest in the above identified patent is vested in the assignee Virginia Commonwealth University, as certified on the attached Certification under 37 C.F.R. § 3.73(b).

IV. I believe David J. **MAYER**, Donald D. **PRICE**, Jianren **MAO**, and John W. **LYLE** to be the original and joint inventors of the subject matter which is described and claimed in U.S. Patent No. 5,556,838 ("the '838 patent") granted on September 17, 1996,and for which a reissue patent is sought on the invention entitled, "**INHIBITING THE DEVELOPMENT OF TOLERANCE TO AND/OR DEPENDENCE ON AN ADDICTIVE SUBSTANCE.**"

V. I have reviewed and understand the contents of the '838 patent, including the claims as amended in any amendment and specifically referred to in this oath or declaration.

VI. I acknowledge the duty to disclose information known to me which is material to patentability as defined in 37 C.F.R. §§ 1.56 and 1.175(a)(7). In compliance with this duty, filed herewith is an Information Disclosure Statement and copies of the references cited therein in accordance with 37 C.F.R. § 1.98.

VII. I hereby offer to surrender U.S. Letters Patent No. 5,556,838 pursuant to 37 C.F.R. § 1.178.

VIII. All errors corrected by this reissue application up to the time of filing the oath or declaration under 37 C.F.R. §1.175 occurred without any deceptive intent on the part of the applicants.

IX. Pursuant to 37 C.F.R. § 1.175(a)(1), I verily believe that the '838 patent is wholly or partly inoperative or invalid by reason of applicants claiming more than they were entitled to claim because of errors which arose without deceptive intention on the part of the applicants.

One error being relied upon as a basis for reissue is applicants claiming more than they were entitled to by including within the scope of claim 1 certain "non-synthetic" NMDA receptor antagonists as a result of a prosecution error by applicants. Applicants limited their claims to "synthetic" non-toxic NMDA receptor antagonists in a preliminary amendment filed on May 19, 1994, to obviate a potential rejection based on U.S. Patent No. 5,183,807 (The Delle Valle patent) during the prosecution of the '838 patent application. However, the claims that contained the "synthetic" limitation were later cancelled and replaced, and applicants inadvertently failed to include the "synthetic" limitation in the claims that issued in the '838 patent.

Another error being relied upon as a basis for reissue includes claiming more than the applicants were entitled to claim by including within the scope of claim 1 of the '838 patent, the combination of morphine and ketamine which is disclosed in Bristow et al., "Subcutaneous ketamine analgesia: postoperative analgesia using subcutaneous infusions of ketamine and morphine," Annals of the Royal College of Surgeons of England, Vol. 71 (1989).

A further reason for amending the claims issued in the '838 patent is the disclosure in the published article by Chapman and Dickenson, entitled "The

Combination of NMDA antagonism and morphine produces profound antinociception in the rat dorsal horn", *Brain Research*, 573 (1992) 321-323. This article discloses a composition containing morphine and 7CK, the latter being described as a "selective antagonist at the glycine site on the NMDA receptor." The compound 7CK is not described as being "nontoxic." The Chapman et al article also suggests that morphine could be combined with either ketamine or AP5 and AP5 is not described as being "nontoxic.". To avoid any issue as to whether the nontoxic substance in the claims of the '838 patent embraces 7CK or AP5, the claims presented in this reissue claims not only exclude ketamine, but also exclude 7CK and AP5 from the nontoxic substance.

Amended independent claim 1 (with added language noted with underlines) and independent reissue claims 3, 4 and 5 correct these errors as follows:

1. *A formulated pharmaceutical composition comprising an addictive substance and at least one nontoxic synthetic substance that blocks the N-methyl-D-aspartate receptor or a major intracellular consequence of N-methyl-D-aspartate receptor activation, and which excludes ketamine, AP-5 and 7-chlorokynurenate, the addictive substance being selected from the group consisting of alfentanyl, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, metazocine, methadone, metopon, morphine, opium extracts, opium fluid extracts, powdered opium, granulated opium, raw opium, tincture of opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan and pharmaceutically acceptable salts thereof.*

3. *A formulated pharmaceutical composition comprising an addictive substance and at least one nontoxic synthetic substance that blocks the N-methyl-D-aspartate receptor and consists essentially of a morphinan or blocks a major intracellular consequence of N-methyl-D-aspartate receptor activation, the addictive substance being selected from the group consisting of alfentanyl, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, metazocine, methadone, metopon, morphine, opium extracts, opium fluid extracts, powdered opium, granulated opium, raw opium, tincture of opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan and pharmaceutically acceptable salts thereof.*

4. *A formulated pharmaceutical composition comprising an addictive substance and a non-toxic synthetic substance, the addictive substance being selected from the group consisting of alfentanyl, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, isomethadone, levorphanol, methadone, morphine, oxycodone, oxymorphone, pethidine, and pharmaceutically acceptable salts thereof, the non-toxic synthetic substance being selected from the group consisting of dextromethorphan, dextrorphan, and pharmaceutically acceptable salts thereof.*

5. *A formulated pharmaceutical composition comprising an addictive substance and a non-toxic synthetic substance, the addictive substance being selected from the group consisting of alfentanyl, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, isomethadone, levorphanol, morphine, oxycodone, oxymorphone, pethidine, and pharmaceutically acceptable salts thereof, the non-toxic synthetic substance being a blocker of the N-methyl-D-aspartate receptor and consisting essentially of morphinans.*

Another error relied upon for this reissue is that it was error for applicants not to provide claims of more intermediate and more narrow scope than the claims that issued in the '838 patent. Accordingly, the following additional dependent claims 6-16 are being added. Newly added claims 15 and 16, include the subject matter of claim 2.

6. *A composition according to claims 1, 3, 4 or 5 wherein the addictive substance is selected from the group consisting of alfentanyl, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, isomethadone, methadone, morphine, oxycodone, oxymorphone, pethidine, and pharmaceutically acceptable salts thereof.*

7. *A composition according to claims 1, 3,4 or 5 wherein the addictive substance is selected from the group consisting of alfentanyl, codeine, dihydrocodeine, fentanyl, isomethadone, methadone, pethidine, and pharmaceutically acceptable salts thereof.*

8. *A composition according to claims 1, 3, 4 or 5 wherein the addictive substance is selected from the group consisting of codeine, methadone, and pharmaceutically acceptable salts thereof.*

9. *A composition according to claims 1, 3, 4 or 5 wherein the addictive substance includes morphine or a pharmaceutically acceptable salt thereof.*

10 *A composition according to claims 1,3,4 or 5 wherein the addictive substance includes oxycodone or a pharmaceutically acceptable salt thereof*

11. *A composition according to claims 1, 3, 4 or 5 wherein the addictive substance includes hydrocodone or a pharmaceutically acceptable salt thereof.*

12. *A composition according to claims 1, 3, 4 or 5 wherein the addictive substance includes oxymorphone or a pharmaceutically acceptable salt thereof.*

13. *A composition according to claims 1, 3, 4 or 5 wherein the addictive substance includes hydromorphone or a pharmaceutically acceptable salt thereof.*

14. *A composition according to claims 1, 3, 4 or 5, in oral dosage form.*

15. *A composition according to claims 3, 4 or 5, in sustained release dosage form.*

16. *A composition according to claims 1, 3, 4 or 5, in oral dosage and sustained release dosage form.*

X. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

XI. I hereby specify the following as the correspondence address to which all communications about this application are to be directed:

SEND CORRESPONDENCE TO: Arnold I. Rady
MORGAN & FINNEGAN, L.L.P.
345 Park Avenue
New York, NY 10154-0053

DIRECT TELEPHONE CALLS TO: Arnold I. Rady (212-758-4800)

XII. I hereby appoint the following attorneys and/or agents with full power of substitution and revocation, to prosecute this application, to receive the patent, and to transact all business in the Patent and Trademark Office connected therewith:

John C. Vassil (Reg. No. 19,098), Alfred P. Ewert (Reg. No. 19,887), David H. Pfeffer (Reg. No. 19,825), Harry C. Marcus (Reg. No. 22,390), Robert E. Paulson (Reg. No. 21,046), Stephen R. Smith (Reg. No. 22,615), Kurt E. Richter (Reg. No. 24,052), J. Robert Dailey (Reg. No. 27,434), Eugene Moroz (Reg. No. 25,237), John F. Sweeney (Reg. No. 27,471), Arnold I. Rady (Reg. No. 26,601), Christopher A. Hughes (Reg. No. 26,914), William S. Feiler (Reg. No. 26,728), Joseph A. Calvaruso (Reg. No. 28,287), James W. Gould (Reg. No. 28,859), Richard C. Komson (Reg. No. 27,913), Israel Blum (Reg. No. 26,710), Bartholomew Verdirame (Reg. No. 28,483), Maria C.H. Lin (reg. No. 29,323), Joseph A. DeGirolamo (Reg. No. 28,595), Michael P. Dougherty (Reg. No. 32,730), Seth J. Atlas (Reg. No. 32,454), Andrew M. Riddles (Reg. No. 31,657), Bruce D. DeRenzi (Reg. No. 33,676), Mark J. Abate (Reg. No. 32,527), John T. Gallagher (Reg. No. 35,516), Steven F. Meyer (Reg. No. 35,613), Kenneth H. Sonnenfeld (Reg. No. 33,285), Tony V. Pezzano (Reg. No. 38,271), Andrea L. Wayda (Reg. No. 43,979) and Walter G. Hanchuk Reg. No. (35,179) of Morgan & Finnegan, L.L.P. whose address is: 345 Park Avenue, New York, New York, 10154; and Michael S. Marcus (Reg. No. 31,727) and John E. Hoel (Reg. No. 26,279) of Morgan & Finnegan, L.L.P., whose address is 1775 Eye Street, Suite 400, Washington, D.C. 20006.

Richard C. Franson, Ph.D.
Director, Office of Technology Transfer
President, VCU – Intellectual Property Foundation
Virginia Commonwealth University

Signature: Richard C. Franson **Date:** 6/15/01

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ASSIGNMENT

WHEREAS, David J. Mayer, of Richmond, VA
Donald D. Price, of Richmond, VA
Jianren MAO, of Richmond, VA

being employees of Virginia Commonwealth University, have invented certain new and useful improvements in an invention entitled:

HIBITING THE DEVELOPMENT OF TOLERANCE TO AND/OR DEPENDENCE ON AN ADDICTIVE SUBSTANCE

for which an application for United States Letters Patent, Serial No. _____ was filed on _____; and

WHEREAS, Virginia Commonwealth University, a corporate instrumentality of the Commonwealth of Virginia, hereinafter referred to as UNIVERSITY, is desirous of acquiring certain rights thereunder; and

WHEREAS, the invention was made using facilities and resources controlled by the UNIVERSITY; and

WHEREAS, Virginia Commonwealth University's Intellectual Properties Policy, which applies to us as employees of Virginia Commonwealth University pursuant to Section 23-4.3.B of the Code of Virginia, provides, among other things, that inventions made using facilities and resources controlled by the UNIVERSITY become the property of the UNIVERSITY, and that UNIVERSITY employee-inventors are obligated to assign their rights in the invention and any patent application(s) and any patent(s) issued thereon to the UNIVERSITY;

NOW, THEREFORE, for one dollar ($1.00) and other good and valuable consideration, receipt of which is hereby acknowledged, We agree to and do hereby sell, assign and transfer unto said UNIVERSITY the entire right, title, and interest in and throughout the United States of America (including its possessions and dependencies) and all countries foreign thereto, in and to said invention (whether patentable or not), and any and all patents (including reissues and extensions thereof), of any country, which have been or may be granted on said invention or any part thereof, or any divisional, substitute, continuation-in-whole or in part, renewal, reissue or other patent application based thereon, and based upon said invention, together with the right of said UNIVERSITY to apply for such patent in its own name in all countries of the world where such is permissible by law, and the right to claim the benefit of the priority right provided by the International Convention of 1883, as amended to date, and any such priority right;

TO BE HELD AND ENJOYED BY said UNIVERSITY, its successors and assigns, to the full ends of the respective terms for which said patents or any of them have been or may be granted as fully and entirely as the same would have been held and enjoyed by us had no sale and assignment of said interest be made;

AND we do hereby authorize and request the Commissioner of Patents of the United States of America to issue any and all United States Patents which may be granted upon said invention or any part thereof, to said UNIVERSITY;

AND we hereby agree for ourselves, and for our heirs, executors and administrators, to execute without further consideration any further lawful documents and any further assurances, and any divisional, continuation-in-whole or in-part, substitute, renewal, reissue, or other applications for patents for any country that might be deemed necessary by said assignee fully to secure to said assignee its interest as aforesaid in and to said invention or any part thereof, and in and to said several patents or any of them;

AND in addition we agree that any and all royalties, rents, payments or any receipts from the sale, assignment, transfer licensing or use of said invention, whether patented or not, which are received by the said UNIVERSITY shall be the property of the UNIVERSITY with the understanding that we will receive a percentage of said royalties, rents, payments, or receipts pursuant to and in accordance with the Virginia Commonwealth University Intellectual Properties Policy as adopted May 20, 1988 or as amended or superseded thereafter;

AND we do hereby convenant for ourselves and our legal representatives and agree with said UNIVERSITY, its successors and assigns that we have granted no right or license to make, use or sell said invention to anyone except said UNIVERSITY, that prior to the execution of this deed our right, title and interest in said invention had not been otherwise encumbered, and that we have not executed and will not execute any instrument in conflict herewith.

Executed this 1st day of April, 1993

Witnessed by: